PART ONE
SULFONAMIDE ANALOGS OF CERTAIN FATTY ACIDS

PART TWO
A METHOD FOR THE RAPID HYDROLYSIS OF SULFONAMIDES

BY

RICHARD EDWIN HECKERT

A.B., Miami University, 1944
A.M., University of Illinois, 1947

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY
IN THE GRADUATE COLLEGE OF THE
UNIVERSITY OF ILLINOIS, 1949

URBANA, ILLINOIS

1949

PART ONE
SULFONAMIDE ANALOGS OF CERTAIN FATTY ACIDS

PART TWO
A METHOD FOR THE RAPID HYDROLYSIS OF SULFONAMIDES

BY

RICHARD EDWIN HECKERT

A.B., Miami University, 1944
A.M., University of Illinois, 1947

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY
IN THE GRADUATE COLLEGE OF THE
UNIVERSITY OF ILLINOIS, 1949

URBANA, ILLINOIS

1949

ACKNOWLEDGMENT

The author wishes to express his appreciation to Professor Harold R. Snyder for his encouragement and invaluable suggestions throughout the course of these investigations.

He is indebted to the Minnesota Mining and Manufacturing Company for the fellowship held since February, 1948.

PART ONE

SULFONAMIDE ANALOGS OF CERTAIN FATTY ACIDS

Introduction

Substances closely related to essential metabolites frequently compete with these materials in chemical transformations necessary to the metabolism of microorganisms. Among the structural modifications sometimes successful in transforming vitamin-like substances into antimetabolites is the replacement of a carboxyl with a sulfonic acid or sulfonamide group (1). In the present work, sulfonamide analogs of a number of fatty acids have been prepared for a study of their bacteriostatic properties.

Discussion Of Results

The sulfonamide, sulfonanilide and sulfonamidopyridine analogs of myristic, palmitic and stearic acids were prepared in excellent yield by the sequence: The corresponding fatty acid, the silver salt, the alkyl bromide of one less carbon atom, the sodium alkylthiosulfate, the sulfonyl chloride and the sulfonamide.

Degradation of the silver salts in dry carbon tetrachloride with bromine afforded the alkyl bromides in yields of 55-65%. The Bunte salts, crystalline and readily purified, were formed nearly quantitatively in boiling 50% ethanol. Suspensions of these salts in aqueous methanol on treatment with chlorine (2) gave the sulfonyl chlorides which were converted to the amides under anhydrous conditions. The sulfonamides are white, crystalline substances melting between 70 and 120°.

9,10-Dichlorostearic acid, from oleic acid, was converted to silver dichlorostearate and subsequently to 1-bromo- and 1-iodo-8,9-dichloroheptadecane. The Bunte salt was prepared with difficulty, but potassium thiocyanate in absolute ethanol gave an excellent yield of 1-thiocyano-8,9-dichloroheptadecane.

A crystalline sulfonamide was not obtained when the product of the chlorination of sodium 8,9-dichloroheptadecyl-thiosulfate or of the thiocyanate was treated with ammonia in absolute ethanol.

9,10,12,13-Tetrachlorostearic acid was prepared by low temperature chlorination of the mixed acids from cottonseed oil. 8,9,11,12-Tetrachloroheptadecane sulfonamide, prepared by the method employing 1-iodo-8,9,11,12-tetrachloroheptadecane and 8,9,11,12-tetrachloroheptadecyl thiosulfate, was not dehalogenated when treated with acetone-sodium iodide reagent.

BIBLIOGRAPHY

1. Roblin, Chem. Rev., 38, 255 (1946).

2. Douglass and Johnson, J. Am. Chem. Soc., 60, 1486 (1938).

PART TWO

A METHOD FOR THE RAPID HYDROLYSIS OF SULFONAMIDES

Introduction

The foremost objection to the Hinsberg method for the separation of primary, secondary and tertiary amines has been the difficulty with which the intermediate sulfonamides were hydrolyzed. This investigation was undertaken in an attempt to find a satisfactory solution to the problem of the inertness of sulfonamides to ordinary hydrolytic agents.

Discussion Of Results

Acid hydrolysis of sulfonamides is usually carried out in 20% hydrochloric acid (1). If the cleavage is successful, the amine is recovered in high yield, the chief disadvantage to the

method being the time required to effect hydrolysis. Because of its higher boiling point, 48% hydrobromic acid was tried with benzenesulfonanilide. The reaction was rapid, but *p*-bromoaniline rather than aniline was the principal constituent of the amine fraction.

A mixture of forty-eight per cent hydrobromic acid and phenol has been found to be an excellent reagent for cleaving sulfonamides when the object is the recovery of the constituent amine. Phenol, in addition to enhancing the solubility of the sulfonamide, serves as an acceptor for the oxidation product, bromine, and prevents bromination of the amine.

Of the variety of types of sulfonamides tried, most were completely hydrolyzed when stirred and refluxed with this reagent for one hour. Included in this group is *p*-nitrobenzenesulfonanilide which was recovered unchanged after thirty-six hours refluxing with twenty-five per cent hydrochloric acid. Sulfonamides derived from ammonia and from an aliphatic amine required longer periods than those of simple aromatic amines. Polymethylated benzenesulfonanilides, such as mesitylene- and durenesulfonanilide, required twenty minutes or less with the new reagent.

The cleavage of the sulfonamide, in addition to hydrolysis, involves to an appreciable extent reduction of the fragment containing sulfur. The method is therefore unsatisfactory if the sulfonic acid is to be recovered.

When, for some reason, hydrobromic acid can not be used, the time required for the hydrolysis of sulfonamides with hydrochloric acid may be considerably shortened by adding phenol.

BIBLIOGRAPHY

1. Schreiber and Shriner, J. Am. Chem. Soc., 56, 1618 (1934).

VITA

The author was born in Oxford, Ohio, on January 13, 1924. His elementary and secondary education was acquired at the William McGuffey Grade and High Schools in that village. He attended Miami University from September, 1941, until July, 1944, at which time he received the degree of Bachelor of Arts. From July, 1944, until June, 1946, he served in the United States Army and during most of this period was associated with the Manhattan Project at Oak Ridge, Tennessee. Since September of 1946, he has been enrolled in the Graduate College of the University of Illinois and received the degree of Master of Arts from this university in August, 1947. During the course of his studies he was employed as a teaching assistant until January, 1948. At that time he was granted the Minnesota Mining and Manufacturing Company Fellowship which was held until June, 1949.

Digitized by the Internet Archive
in 2026

https://archive.org/details/IA41549807_0065